Comments of The Humane Society of the United States
on the NIEHS' *Guidance Document on Using In Vitro Data to Estimate In Vivo Starting Doses for Acute Toxicity*

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These comments are being submitted on behalf of The Humane Society of the United States (HSUS) and our nearly 7 million members and constituents. We thank the National Institute on Environmental Health Sciences (NIEHS) for the opportunity to comment on the *Guidance Document on Using In Vitro Data to Estimate In Vivo Starting Doses for Acute Toxicity*.

In September of 2000, the NIEHS convened an International Workshop on In Vitro Methods for Assessing Acute Systemic Toxicity in Arlington, Virginia. Its purposes were to: 1) assess the current validation status of *in vitro* test methods that might be useful for assessing the acute systemic toxicity potential of chemicals, and 2) develop recommendations for future research, development, and validation studies that might further enhance the use of *in vitro* methods for this purpose.

In August of 2001, The NIEHS published two documents based on this workshop: the *Report of the International Workshop on In Vitro Methods for Assessing Acute Systemic Toxicity* and the *Guidance Document on Using In Vitro Data to Estimate In Vivo Starting Doses for Acute Toxicity*. The workshop report provides conclusions and recommendations from the invited expert scientists, based on their evaluations at the workshop. The Guidance Document provides Standard Operating Procedures (SOPs) for performing two *in vitro* basal cytotoxicity assays and describes how to use this non-animal data to predict starting doses for *in vitro* oral acute toxicity studies.

The HSUS commends the NIEHS for convening the international workshop, issuing the subsequent reports, and recommending that *in vitro* basal cytotoxicity assays be adopted as a means of predicting starting doses for *in vivo* acute oral toxicity tests. The implementation of this recommendation will serve to reduce the number of animals used in *in vivo* procedures such as the Up and Down Method and the Acute Toxic Class Method.

The HSUS urges the NIEHS to move swiftly in encouraging the use of cytotoxicity assays as initial steps in acute toxicity testing. Further, we urge the NIEHS to take a leadership role in systematically collecting and evaluating newly generated *in vitro* and in *vivo* data on acute toxicity testing. This coordinating role will generate the data necessary to inspire widespread confidence in using *in vitro* data to estimate the proper starting doses in *in vivo* testing.

More importantly, these *in vitro*/*in vivo* comparisons will facilitate the implementation of *in vitro* cytotoxicity testing as a full replacement of *in vivo* acute toxicity testing. We urge the NIEHS to use its expertise and resources to swiftly validate such *in vitro* testing as the stand-alone procedure for acute toxicity testing.

The HSUS will be urging the Environmental Protection Agency (EPA) to immediately incorporate basal cytotoxicity testing into its High Production Volume (HPV) chemical testing program, as a means of reducing animal testing for acute toxicity testing. A swift incorporation

would be in keeping the with the Administration's October 1999 agreement with the animal protection community.

The HSUS urges the NIEHS to make the elimination of animal use in acute systemic toxicity testing a high priority. Animals have been suffering and dying in the LD50 Test and its subsequent refinements since the 1920s. We respectfully request your serious consideration of our comments.